Complete Summary

GUIDELINE TITLE

Optimization of surgical and pathological quality performance in radical surgery for colon and rectal cancer: margins and lymph nodes. Guideline recommendations.

BIBLIOGRAPHIC SOURCE(S)

Smith AJ, Driman DK, Spithoff K, McLeod R, Hunter A, Rumble RB, Langer B, Expert Panel on Colon and Rectal Cancer Surgery and Pathology. Optimization of surgical and pathological quality performance in radical surgery for colon and rectal cancer: margins and lymph nodes. Guideline recommendations. Toronto (ON): Cancer Care Ontario (CCO); 2008 Apr 17. 65 p. (Evidence-based series; no. 17-4). [132 references]

GUIDELINE STATUS

This is the current release of the guideline.

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the <u>Cancer Care Ontario Web site</u> for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Curable colon and rectal cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness Management Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery Oncology Pathology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate the recommended technique and extent of surgical resection for curable colorectal cancer (CRC), including extent of bowel resection, extent of lymph node resection, and reporting requirements
- To evaluate the recommended approach to processing and reporting the resected specimen, including specimen marking in the operating room, as well as processing and reporting requirements in the pathology laboratory

TARGET POPULATION

All patients with curable colon¹ and rectal² cancer in whom surgical management with radical excision is undertaken. This may include selected patients with M1 disease.

Note: This document does not apply to patients with primary cancers that are managed by polypectomy or full thickness transanal excision, patients treated for recurrent tumours, or patients undergoing surgery with palliative intent.

- 1. For the purpose of this document, colon cancers are defined as those that lie within the large intestine from the cecum to the top of the rectum.
- 2. Rectal cancers are defined as adenocarcinomas that lie between the termination of the sigmoid colon, usually at the level of the sacral promontory, and the dentate line. The mesorectum and its enveloping mesorectal fascia end at the pelvic floor or top of the puborectalis sling, while the most distal aspect of the rectum ends at the dentate line. The rectum is divided into three sections: lower rectum (0-5 cm from anal verge), mid rectum (5-10 cm from anal verge) and upper rectum (10-15 cm from anal verge). Rectal tumors are classified according to their location relative to the peritoneal reflection anteriorly, i.e., entirely above, astride or entirely below the peritoneal reflection.

INTERVENTIONS AND PRACTICES CONSIDERED

- 1. Colon and rectum resection to establish negative margins (i.e., margins free of residual tumor)
- 2. Total mesorectal excision
- 3. En bloc multivisceral resection
- 4. Documentation of inadvertent tumour perforation

- 5. Lymphadenectomy
- 6. Histopathological examination and reporting

MAJOR OUTCOMES CONSIDERED

- Disease-free survival
- Local recurrence
- Overall survival
- Margin status

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources) Hand-searches of Published Literature (Secondary Sources) Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

The MEDLINE database (1999 to February week 1, 2007) was systematically searched for evidence, using the following Medical Subject Heading (MeSH) terms "colonic neoplasms/su,pa", "rectal neoplasms/su,pa", "colorectal neoplasms/su,pa", "intestinal perforation", and "lymph node excision". These MeSH terms were combined with text words for margins of resection, en bloc multivisceral resection, inadvertent tumour perforation, total mesorectal excision, and lymphadenectomy. The results were limited by using search words for the following publication types: randomized controlled trials, prospective studies, case-series, retrospective studies, and pathology studies. Personal reprint files were also searched and citations from retrieved articles were reviewed.

Inclusion Criteria

Studies were considered eligible for inclusion if they were:

- 1. Randomized controlled trials (RCTs), non-randomized prospective studies, case-series or retrospective reviews reporting relevant outcome data for patients undergoing surgical resection for primary colon or rectal cancer.
- 2. Syntheses of evidence in the form of systematic reviews or meta-analyses.
- 3. Published in the English language.

Exclusion Criteria

Studies were not considered for inclusion if they were:

- 1. Case reports or narrative review articles
- 2. Studies of patients undergoing surgical resection for recurrent colon or rectal

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

No data were pooled in a meta-analysis due to the absence of randomized data and the heterogeneity of the included studies in terms of patients, surgery and pathology procedures, measurements of outcomes, and choice of outcome comparisons.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The evidence currently available in the literature on surgical and pathology quality performance is primarily comprised of retrospective reviews of charts or databases, case series, subgroup or exploratory analyses of randomized controlled trials (RCTs), and non-randomized prospective studies. In developing the recommendations in this report, the Expert Panel on Colon and Rectal Cancer Surgery and Pathology took into consideration existing guidelines and key papers in the field in addition to studies published since 1999. The available studies were often small and likely underpowered to detect differences in outcome between patient subgroups, and details regarding surgical and pathology methods were often poorly reported. In addition, results were complicated by confounding factors, varying statistical methods to detect associations between surgical and pathological variables and outcome, and varying comparisons. Where evidence was not available or was not sufficient to reach definitive conclusions, recommendations are based on the expert opinion of the panel.

See the discussion section of the original guideline document for a full description of the methods used to formulate the recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Report Approval Panel

Prior to the submission of this evidence-based series (EBS) draft report for external review, the report was reviewed and approved by the Program in Evidence-Based Care (PEBC) Report Approval Panel, which consists of two members, including an oncologist, with expertise in clinical and methodology issues. Key issues raised by the Report Approval Panel and the modifications made by the guideline authors in response to the feedback are provided in the original guideline document.

External Review by Ontario Clinicians

Following the review and discussion of Section 1: Recommendations and Section 2: Evidentiary Base of this EBS in the original guideline document and review and approval of the report by the PEBC Report Approval Panel, the Expert Panel on Colon and Rectal Cancer Surgery and Pathology circulated Sections 1 and 2 to external review participants in Ontario for review and feedback.

Methods

Feedback was obtained through a mailed survey of 168 external review participants in Ontario (92 surgeons, 48 pathologists, 12 radiation oncologists, and 16 medical oncologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The survey was mailed out on December 10, 2007. Follow-up reminders were sent at four weeks (post card) and six weeks (complete package mailed again). The Expert Panel on Colon and Rectal Cancer Surgery and Pathology reviewed the results of the survey.

The EBS report reflects the integration of feedback obtained through the external review process with final approval given by the Expert Panel on Colon and Rectal Cancer Surgery and Pathology and the Report Approval Panel of the PEBC.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations have been organized under two categories: Surgical Issues and Pathology Issues. The foundation for the surgical recommendations is the Guidelines 2000 document sponsored by the National Cancer Institute (NCI). This report reviews the evidence on surgical issues up to 1999 and provides recommendations based on the reviewed evidence. Section 2 in the original guideline document contains the systematic review of the evidence from 1999 to 2007 that was undertaken to supplement the NCI guideline. Where evidence is lacking, the recommendations are based on the consensus of the panel. Recommendations for the pathology issues are based on a systematic review of the published literature up to 2007, as well as a review of four key papers in the field, also presented in Section 2 in the original guideline document. The outcomes of interest behind the recommendations are local recurrence, disease-free survival, and overall survival.

The following recommendations are offered by the Expert Panel on Colon and Rectal Cancer Surgery and Pathology:

Staging Definitions

 The Tumour, Node, Metastasis (TNM) classification of tumours described by the American Joint Committee on Cancer (AJCC) is recommended for tumourstaging definitions.

Tumour Extent and Margin Guidelines

- Resections and Positive Resection Margin Definitions
 - American Joint Committee on Cancer categorizes resections as R0: no residual tumour; R1: microscopic residual tumour; R2: macroscopic residual tumour.
 - Presence of tumour 1 mm or less from a margin should be considered a positive resection margin.
- Surgeons must preoperatively consider the expected R status at the end of an operation. Clinical (e.g., evidence of tumour tethering or fixation on physical exam) and radiological (e.g., cross-sectional imaging with magnetic resonance imaging [MRI] or computed tomography [CT]) assessment is necessary to identify lesions that may have a threatened or involved radial margin. Patients with such a presentation should be considered for neoadjuvant therapy (See Related Guidelines in the original guideline document).
- Close consultation between the surgeon and the pathologist is required in the assessment of margins.

Surgery

Margins of Resection: Colon

Key Recommendation

• Negative margins are the goal of colon resection

Technical Recommendations

Technical recommendations are based on Expert Panel consensus and endorsement of the NCI Guidelines 2000 and, for recommendations for radial margins, evidence supporting en bloc resection with negative margins for adherent tumours.

Proximal and Distal Margins

• The primary determinant of the extent of bowel resection is the need for adequate removal of lymph nodes and arterial supply that is consistent with the creation of a well-vascularized anastomosis. An adequate minimum length for proximal and distal colon resection margin is 5 cm, although they are generally much greater.

Radial Margins

- Radial, non-peritonealized negative resection margins of the colon should be
 obtained and must be histologically free of disease (R0) to achieve a curative
 resection. This does not apply to surfaces of the colon where the tumour has
 penetrated through a free serosal surface but is not adherent to adjacent
 structures.
- Ideally, locally advanced adherent tumours should be diagnosed preoperatively through appropriate application of cross-sectional imaging, especially computed tomography scanning, and should be assumed to be malignant in curative-intent operations. En bloc resection of adherent organs or parts of organs should be done where possible to obtain a R0 excision (See En Bloc Multivisceral Resection below).
- The specimen must be labelled and areas of possible radial margin involvement, particularly segments not typically associated with a radial margin (e.g., transverse colon), should be marked for correct identification by the pathologist.

Margins of Resection: Rectum

Key Recommendation

Negative margins are the goal of rectal resection

Technical Recommendations for Proximal and Distal Margins

Technical recommendations are based on the Expert Panel consensus informed by the NCI Guidelines 2000 and evidence emerging in the recent literature update. No data were found to inform proximal rectal resection margin lengths. Distal margin length of 2 cm or greater and a minimally acceptable distal margin length of 1 cm were recommended by the NCI Guidelines 2000. The evidence update yielded 19 studies reporting clinical outcomes by distal margin length or distal tumour spread and provided conflicting findings for adequate distal margin length, ranging from 1 cm to 4 cm.

Proximal Margins

• The primary determinant of the extent of resection of proximal rectum is determined by technical considerations for obtaining adequate lymphadenectomy and reconstruction. The resection margin length should be a minimum 5 cm.

Distal Margins

- The main determinants of distal margin length are adequate clearance of intramural cancer spread and adequate removal of lymph nodes in pericolic fat.
- The distal margin length should be measured in the fresh, anatomically restored ex vivo condition immediately after removal.
- The distal aspect of the tumour should be marked or carefully measured at the time of initial assessment, recognizing that this may change following preoperative therapy.
- For tumours of the proximal and mid rectum, the distal margin length should be a minimum of 5 cm from the distal edge of the primary tumour in most patients to remove positive lymph nodes that are distal to the palpable leading edge of the tumour. The mesorectum and bowel edge must be transected transversely to avoid coning towards the distal resection margin and possible loss of lymph node tissue distal to the primary tumour.
- For tumours at or below the end of the mesorectum, ideally a distal margin length of 2 cm in the fresh specimen should be obtained, not including the circular stapler donut. In expert hands, a negative margin of less than 2 cm can be oncologically adequate to facilitate very low colorectal re-anastomosis. A negative distal margin must not be compromised in an effort to avoid a permanent colostomy. Please see Section 2 in the original guideline document for a full discussion of this issue.
- Intraoperative evaluation of the distal margin by a pathologist may be beneficial but shortcomings of this procedure (e.g., false negative results) must be recognized.

General

- Abdominoperineal resection (APR) is indicated for patients in whom the rectal tumour invades or very closely encroaches upon the external anal sphincter.
- The surgeon should scrupulously and systematically document details relevant to the proximal and distal margins on the operative report.
- It is common practice to submit the circular stapler donuts for histological examination; however, histology of the donuts should not be relied on to determine margin status.

Technical Recommendations for Circumferential Radial Margins

These recommendations are informed by numerous retrospective studies and case series cited in the NCI Guidelines 2000 and the updated literature search that demonstrated the importance of negative circumferential radial margins (CRM) to minimize local recurrence and increase disease-free survival and overall survival.

- A CRM is present in the mid-lower rectum, while the upper rectum has a
 peritonealized anterior surface and a non-peritonealized posterior radial
 margin similar to the ascending and descending colon.
- All rectal cancers should undergo preoperative workup to assess the extent to which the CRM is threatened. This includes pelvic computed tomography or magnetic resonance imaging and, for lesions within reach of the examining finger, a digital rectal exam.
- For lesions that are stage II (i.e., T3 or T4) or III (i.e., likely positive lymph nodes on cross sectional imaging), neoadjuvant therapy should be considered. Such determinations demand a high-quality magnetic resonance imaging and, ideally for T status, a trans-rectal ultrasound (See Related Guidelines in the original guideline document).
- Adherent rectal cancers should be diagnosed preoperatively and en bloc resection may be required to obtain an R0 resection in such cases (See En Bloc Multivisceral Resection below).
- The technique of total mesorectal excision (TME) should be employed (See Total Mesorectal Excision below).
- The CRM is positive if the tumour is located 1 mm or less from the cut edge of the specimen.
- The surgeon should scrupulously and systematically document details relevant to the CRM on the operative report.

Total Mesorectal Excision

Key Recommendations

 For rectal cancer, the technique of total mesorectal excision using sharp dissection under direct visualization in the plane between the parietal fascia of the pelvis and the visceral fascia of the mesorectum should be performed. Careful dissection in this plane offers protection to the pelvic autonomic nerves, which run under the parietal fascia, and offers the best chance for local tumour control.

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000.

- The goal of surgery should be wide anatomic resection to obtain radial clearance of the primary tumour and lymphatic, vascular, and perineural tumour deposits in the mesorectum, preserving the integrity of the mesorectal fascia propria.
- There is evidence that tumours rarely extend in the bowel wall distal to their palpable edge, but deposits in lymph nodes 2-4 cm distal to the palpable edge of a tumour have been observed in a low percentage of cases.
- While tumours of the high rectum do not require total mesorectal excision, in all cases at least 5 cm of mesorectum distal to the leading edge of the tumour should be removed if possible.
- Coning-in, or breaching the visceral fascia proximal or just distal to the tumour, should be avoided in both partial and total mesorectal excision to ensure the removal of all mesorectal nodes that are up to 5 cm distal to the leading edge of the tumour.

En Bloc Multivisceral Resection

Key Recommendations

Locally advanced, adherent colorectal tumours should be dissected en bloc
with histologically negative margins for resection to be considered adequate.
If a tumour is transected at the site of local adherence, resection is not
complete.

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000.

• If a surgeon finds a locally advanced, adherent tumour in an otherwise curable patient and is not prepared to perform a multivisceral resection, then consideration should be given to either aborting the operation or creating a proximal stoma and then referring the patient for multidisciplinary opinion regarding possible neoadjuvant therapy and more radical surgery.

Inadvertent Tumour Perforation

Key Recommendation

• Every effort should be made to avoid inadvertent perforation of the colon or rectum during dissection.

<u>Technical Recommendation</u>

The technical recommendation is based on the Expert Panel consensus informed by the evidence demonstrating a worse outcome for patients with inadvertently perforated tumours.

• Inadvertent perforation should be documented in the operative report and the pathology requisition form.

Pathology

Margins of Resection: Colon

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in four key papers in the field, as well as pathology studies identified in the recent literature search.

Proximal and Distal Margins

• The surgeon should communicate with the pathologist regarding the orientation of the specimen.

- Proximal and distal margins should be sampled for histological examination.
- The distance of the tumour to the proximal and distal margins should be reported in the fresh state, if possible. Measurement in the fixed state must take into account the fact that shrinkage will have occurred; pinning the fresh specimen to a board, under tension, will produce less shrinkage. If the tumour is close to a margin, the distance between the tumour and the margin of concern should be reported as measured microscopically on the glass slide.

Radial Margins

- The surgeon must clearly indicate to the pathologist areas with close contact to other organs or the abdominal wall. The pathologist should be aware of the retroperitoneal margin that exists in certain locations (e.g., proximal ascending colon and descending colon).
- The radial margins of the resected specimen should be inked and sectioned.
- The radial margin distance must be reported. The radial margin should be reported as positive if tumour is located 1 mm or less from the inked nonperitonealized surface of the specimen.

Margins of Resection: Rectum

Technical Recommendations

Technical recommendations are based on the Expert Panel consensus informed by the technical issues highlighted in four key papers in the field, as well as pathology studies identified in the recent literature search.

Proximal and Distal Margins

- Proximal and distal margins should be sampled for histological examination.
- Pathologists should pay close attention to mesorectal soft tissue, in addition to the mucosa, when assessing the distal margin.

Circumferential Radial Margins

- All rectal cancer specimens should be assessed grossly by the pathologist using the method developed by a group of researchers.
- The mesorectal tissue that constitutes the CRM, including all non-peritonealized bare areas anteriorly and posteriorly, should be inked. The specimen should be fixed with the tumour segment unopened 5 cm above and below the proximal and distal edges of the tumour, respectively, and a gauze wick placed into the unopened segment to facilitate fixation. Following at least 48 hours of fixation, the segment with the tumour should be sliced into transverse sections. The relationship of the tumour to the CRM must be carefully assessed.
- The CRM distance must be reported. The CRM is positive if the tumour is located 1 mm or less from the margin; this includes tumour cells within a lymph node, vein, or nerve, as well as direct tumour extension.
- Note that tumours of the upper rectum have a peritonealized anterior surface and a non-peritonealized posterior radial margin similar to the ascending and descending colon.

Serosal Penetration

- Involvement of the serosa by tumour (pT4b) is not equivalent to involvement of the radial margin by tumour (although there are circumstances in which an advanced tumour has penetrated the serosa and is adherent to adjacent soft tissue).
- Documentation of serosal involvement by tumour requires careful gross and microscopic examination and may require extensive sampling and/or serial sectioning of sampled tissue blocks.
- Serosal penetration is defined as occurring when any of the following criteria are met:
 - Free tumour cells are present on the serosal surface with underlying ulceration.
 - Tumour is present at the serosal surface with an associated inflammatory reaction, mesothelial hyperplasia, and/or erosion or ulceration.
 - The tumour is close to, but not at the serosal surface but there is an associated mesothelial inflammatory and/or hyperplastic reaction.
- Serosal penetration is an independent prognostic variable and has a strong negative impact on prognosis. The frequency of distant metastasis is greater in cases with perforation of the visceral peritoneum compared to cases with direct invasion of adjacent organs or structures without perforation of the visceral peritoneum, and the median survival time following surgical resection for cure is shorter for patients with pT4b tumours compared to those with pT4a tumours (with or without distant metastasis).

Lymph Node Assessment

Surgery

Extent of Lymphadenectomy

Technical Recommendations

Technical recommendations are based on Expert Panel consensus informed by the technical issues highlighted in the NCI Guidelines 2000 and evidence suggesting no significant benefit for high arterial ligation over low ligation.

- The goal of colon resection is the removal of the segment of the bowel with the tumour and all the mesentery containing the blood supply and the lymphatics at the level of the primary feeding arterial vessel (e.g., ileocolic, middle colic, left colic, inferior mesenteric artery, and all their branches). When the primary tumour is equidistant from two feeding vessels, both vessels should be excised close to their origin. More radical lymphadenectomy is not supported by available evidence.
- In curative operations, lymph node resection should be en bloc with the main vessel supplying the involved segment of colon.
- Lymph nodes at the origin of feeding vessels (apical nodes) should be included when feasible and tagged for pathologic evaluation.
- Appropriate proximal lymphatic resection and total mesorectal excision of the rectum provides adequate lymphadenectomy for rectal cancer. There is a lack of evidence about the benefit of ligating the inferior mesenteric artery (IMA)

- at its origin at the aorta, although nodes should be removed as high as technically possible to allow for complete removal of clinically involved nodes. Suspicious periaortic nodes should be biopsied for staging.
- The surgeon should report the named vessel and lymph node basin resected en bloc. Clinically suspicious nodes should be reported, and any lymph nodes outside the resected basin that are suspicious and biopsied should be reported.

Number of Lymph Nodes Assessed

Technical Recommendations

Technical recommendations are based on Expert Panel consensus and an endorsement of the recommendation in the NCI Guidelines 2000 and are informed by evidence from a published systematic review and a review of the recent literature indicating an improved survival the greater the number of lymph nodes evaluated.

• In general, and particularly for T3/4 neoplasms, a minimum of 12 lymph nodes should be examined to adequately stage colon and rectal cancer, although an effort should be made to identify all lymph nodes. Importantly, the 12-lymph node target may not be achievable in patients with T1 or T2 tumours and/or some patients who receive neoadjuvant therapy.

Pathology

Technique of Lymph Node Examination

Technical Recommendations

Technical recommendations are based on Expert Panel consensus informed by four key papers in the field and pathology studies identified in the recent literature search.

- Pericolic fat should be carefully examined using inspection and palpation. For colonic tumours, examination should occur after pericolic fat has been stripped off the colon and after any appropriate sections have been taken to evaluate the radial margin.
- In the case of rectal tumours, the cross-sectioned slices are examined for lymph nodes, taking care not to double count lymph nodes that might be present in more than one cross-sectional slice.
- All lymph nodes present must be examined histologically. Nodal examination
 must not stop once 12 nodes have been identified. It is particularly important
 to find small lymph nodes close to the underlying bowel wall. If less than 12
 lymph nodes are found, consideration should be given to placing the fat into a
 lymph node highlighting solution.
- All grossly negative or equivocal lymph nodes must be submitted in their entirety. However, if a node is grossly positive, partial submission is acceptable.

Number of Lymph Nodes Assessed

Technical Recommendations

- Technical recommendations are based on Expert Panel consensus informed by four key papers in the field and pathology studies identified in the recent literature search.
- The pathology report should indicate the number of positive lymph nodes as well as the total number of nodes assessed.
- The number of lymph nodes involved by micrometastases (tumour deposits >0.2 mm but <2.0 mm) and isolated tumour cells (ITCs) (single cells or clusters 0.2 mm or less) should be reported separately from typical (macro) metastases. In cases where there are typical (macro) metastases, micrometastases or ITCs do not change the pN stage. Micrometastases without typical (macro) metastases detected by routine histology are reported as pN1, whereas immunohistochemical detection is reported as pN0. The presence of ITCs does not change the pN classification. Note that special measures to detect micrometastases or ITCs (e.g., multiple tissue levels of paraffin blocks, immunohistochemistry [IHC], polymerase chain reaction [PCR]) are not recommended for the routine examination of regional lymph nodes.</p>
- A tumour nodule in the pericolonic/perirectal fat without histologic evidence of residual lymph node tissue is classified as a lymph node replaced by tumour if the nodule has the form and smooth contour of a lymph node. If the nodule has an irregular contour, the nodule should be classified as a discontinuous extramural extension, pT3 (based on the American Joint Committee on Cancer/International Union Against Cancer Tumour, Node, Metastasis [AJCC/UICC TNM] 6th edition).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

- The National Cancer Institute Guidelines 2000 forms the basis for the surgical components of this document.
- In addition, the recommendations are based on retrospective reviews of charts or databases, case series, subgroup analyses of randomized controlled trials (RCTs), and non-randomized prospective studies.
- Where evidence is lacking, the recommendations are based on the consensus of the panel.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

 Appropriate surgical and pathological management of margins and lymph nodes for patients with colon and rectal cancer following radical surgery to improve outcomes.

- The National Cancer Institute (NCI) Guidelines 2000 cited numerous studies demonstrating better outcome for patients with margins free of residual tumour.
- In the recent literature, one retrospective study demonstrated no significant association between proximal or distal margin lengths and local recurrence or disease-free survival.
- In the recent literature, retrospective and prospective studies reported decreased local recurrence rates and increased survival in patients with negative margins compared with positive margins.
- Five out of seven studies comparing total mesorectal excision (TME) to conventional resection reported decreased local recurrence rates in patients who underwent TME.
- Retrospective reviews and case series demonstrated acceptable outcome in patients who underwent en bloc multivisceral resection of adherent tumours when negative resection margins were achieved.
- One large study of registry data reported improved overall survival for colon and rectal cancer patients who had multivisceral resection of locally advanced adherent colorectal cancer compared to standard resection.
- Several retrospective reviews and database audits demonstrated increased local recurrence and decreased survival in patients who had inadvertent perforation of the bowel.

POTENTIAL HARMS

- Partial or total removal of the urinary bladder as part of the en bloc resection is associated with increased morbidity
- Inadvertent tumour perforation during surgery
- Anastomotic dehiscence

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Smith AJ, Driman DK, Spithoff K, McLeod R, Hunter A, Rumble RB, Langer B, Expert Panel on Colon and Rectal Cancer Surgery and Pathology. Optimization of surgical and pathological quality performance in radical surgery for colon and rectal cancer: margins and lymph nodes. Guideline recommendations. Toronto (ON): Cancer Care Ontario (CCO); 2008 Apr 17. 65 p. (Evidence-based series; no. 17-4). [132 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Apr 17

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Expert Panel on Colon and Rectal Cancer Surgery and Pathology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Dr. Andy Smith, Chair, Surgical Oncologist, Odette Cancer Centre, Sunnybrook; Dr. David Driman, Chair, Pathologist, London Health Sciences Centre; Dr. Bernard Langer, Consultant, Cancer Care Ontario; Dr. Robin McLeod, Surgical Lead, Quality Improvement, Cancer Care Ontario; Karen Spithoff, Research Coordinator, Program in Evidence-based Care; Amber Hunter, Quality Coordinator, Cancer Care Ontario; Dr. Nancy Baxter, Surgical Oncologist, St. Michael's Hospital; Dr. Paul Belliveau, Surgical Oncologist, Hotel-Dieu Hospital; Linda Boich, Vice President Clinical Services, Niagara Health System; Dr. Mahmoud Khalifa, Pathologist, Odette Cancer Centre, Sunnybrook; Dr. Angus Maciver, Surgical Oncologist, Stratford General Hospital; Dr. Craig McFadyen, Surgical Oncologist, Grand River Regional Cancer Centre; Dr. Ken Newell, Pathologist, Grey Bruce Health Services; Bryan Rumble, Research Coordinator, Program in Evidence-based Care; Dr. Marko Simunovic, Surgical Oncologist, Hamilton Regional Cancer Centre

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Expert Panel on Colon and Rectal Cancer Surgery and Pathology who were involved in the writing of this document were polled for potential conflicts of interest.

No conflicts were declared.

GUIDELINE STATUS

This is the current release of the guideline.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the <u>Cancer Care Ontario Web site</u>.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

• Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI Institute on August 27, 2009.

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